International Journal of Scientific Reports
Sekabira R et al. Int J Sci Rep. 2024 Aug;10(8):286-295
http://www.sci-rep.com
pISSN 2454-2156 | eISSN 2454-2164

DOI: https://dx.doi.org/10.18203/issn.2454-2156.IntJSciRep20241993

Review Article

A clinical research site pharmacy for the division of AIDS sponsored clinical trials in a low middle income country

Rogers Sekabira*, Godwin Murungi, Nigel Okot Kinyera, Muzamil Nsibuka Kisekka, Violet Korutaro, Patricia Ntege Nahirya, Adeodata R. Kekitiinwa

Baylor College of Medicine Children's Foundation Uganda, Kampala, Uganda

Received: 09 May 2024
Accepted: 08 July 2024

***Correspondence:**
Dr. Rogers Sekabira,
E-mail: rsekabira@baylor-uganda.org/rsekabira7@gmail.com

ABSTRACT

This review article provides information on the role of clinical research site (CRS) Pharmacies in supporting the division of AIDS (DAIDS)-sponsored clinical trials at the CRS, their legislative framework, and how they differ from community pharmacies. These pharmacies are relatively few, and little information is available about their operation, setup, and requirements in low-and middle-income countries (LMICs). The information in this article is pertinent to pharmacy associations and regulators who formulate policies and guidelines and to pharmacy professionals eager to enhance their skills and competencies through knowledge sharing to improve the quality of healthcare services. Moreover, this information is relevant in establishing a CRS pharmacy and understanding its interaction with various administrative and financial institutions. This article provides information on how CRS pharmacies achieve uninterrupted power supply for investigational medicinal products (IMP) throughout the year, the sponsor and regulatory requirements for the CRS pharmacy and the processes for IMP shipment, from its dispensation to the study participants. The article also provides information on quality control and assurance processes for maintaining a CRS pharmacy. CRS pharmacies in LMICs have unique requirements, operations, services, and setups, and regulatory authorities must develop policies and guidelines that align with these distinct features. More so, leveraging the existing CRS pharmacies to disseminate skills and knowledge to trainees, community pharmacies, and other medicine outlets can significantly enhance the quality of health services delivered to the community.

Keywords: CRS, CRS pharmacy, Clinical trials, DAIDS, Research pharmacists, Community pharmacy, Pharmacist

INTRODUCTION

Pharmacy practice is dynamic, varies across settings, and over time.[1-5] Roles of pharmacists have been recognised and well demonstrated in manufacturing, compounding, academia, and community practice, but not much in clinical research.[6,7] Some authorities still consider pharmacists in clinical research and community practices similar, yet they differ in operations and services.[8]

Uganda has over 2869 licensed medicine outlets; 905 (30%) are wholesale pharmacies, and the rest are retail.[9] Four research pharmacies in Uganda support the US national institutes of health (NIH) DAIDS networks at affiliated clinical research sites (CRS) to conduct investigational new drug (IND) studies of novel treatment and prevention of HIV. The networks include the HIV prevention network (HPTN), the AIDS clinical trials group (ACTG) network and the international maternal pediatrics adolescent AIDS clinical trials (IMPAACT) network.[10] CRS Pharmacies' operations, set-up, and requirements differ from community (wholesale or retail) pharmacies; these differences are not outlined in the current regulatory policies or the country-specific guidelines.[8,11]

Still, pharmacists' roles and responsibilities in CRS pharmacies are unique. They range from identifying protocol pharmacy needs, preparing sponsor monitoring and inspection visits, preparing and completing the investigator's pharmacy file, and pharmacy-specific regulatory activities to closure activities.[12,13] There is a lack of information about CRS pharmacies for CRSs and how they differ from community pharmacy outlets in the country.

In this article, we discuss the role of the CRS Pharmacy in supporting DAIDS-sponsored clinical trials at the CRS, the legislative framework and how it differs from a community pharmacy.

ROLE OF THE CRS PHARMACY IN SUPPORTING DAIDS-SPONSORED CLINICAL TRIALS AT THE CRS

The CRS pharmacy is an investigational medicine product (IMP) repository. It is where the storage, preparation, and dispensing of IMPs occur. The CRS pharmacy should have unique requirements for power supply, staffing, set-up, operation, and conducting of blinded studies. The DAIDS pharmaceutical affairs branch (PAB) instructions and guidelines for conducting DAIDS-sponsored clinical trials list most requirements.[14]

DAIDS requires that the CRS leader delegate the responsibility of managing study products to a trained and registered pharmacist, the pharmacist of record (PoR). The PoR is supported by the associate pharmacists (AP) registered with the pharmacy board at the ministry of health. In the absence of a PoR, APs can perform all the PoR's roles and responsibilities in a clinical trial. These pharmacy staff are the custodians of the CRS pharmacy. The principal investigator should ensure that the PoR is knowledgeable about the protocol, the manual of operations, study-specific procedures, and applicable laws and regulations.

The principal investigator should also establish a mechanism to relay protocol-related information to the PoR. On the other hand, the PoR is responsible for ensuring that this information is communicated to the pharmacy staff and that a system is in place for reporting any incidents or protocol deviations to the principal investigator and the DAIDS PAB.

POSITION OF THE CRS PHARMACY IN SUPPORTING DAIDS-SPONSORED CLINICAL TRIALS

The US department of health and human services (HHS) runs various programs, including the NIH, the office for human research protections (OHRP), and the centres for disease control and prevention (CDC), to promote health and well-being. While the other agencies have a broader focus, the NIH's primary focus is conducting biomedical and public health research, mainly by supporting its institutes and centres, including the national institute of allergy and infectious diseases (NIAID), under which DAIDS functions.

The CRS interacts with its sponsors, NIAID/DAIDS, through various players during DAIDS-sponsored research, Figure 1. These include the office of clinical site oversight (OCSO), the PAB, the DAIDS clinical laboratory operations team (DCLOT), and the clinical trials unit (CTU). The OCSO is a department within DAIDS that monitors the CRS to ensure that clinical research is conducted according to the GCP principles. The PAB, also a part of OCSO, provides expertise on all pharmaceutical aspects of protocol development.[15] The clinical research products management center (CRPMC) supports PAB by supplying, packaging, and distributing study products for all the DAIDS-sponsored clinical trials at the CRS. The DCLOT oversees laboratory establishment, implements laboratory policies, evaluates laboratory performance, and addresses laboratory-related issues. The funded networks work closely with the DCLOT point of contact to provide oversight and solve any protocol-related laboratory issues. Finally, DAIDS uses the CTU as an administrative entity for implementation. The CTU is affiliated with one or more CRSs and contributes to the network clinical research plan by conducting clinical research. The CTU ensures that the CRS is conducting clinical research following the bylaws, applicable regulations and guidelines and that there are active community engagements and participation in the network activities. CTU supports the CRSs during all phases of the life cycle of a protocol, from development, start-up, implementation, and reporting. All clinical research at the CRS is conducted in accordance with the good clinical practice (GCP) principles.[16,17]

Understanding the relationship between the CRS and the CRS pharmacy is essential. The CRS is a discrete location supported by NIAID where qualified professionals conduct clinical research following GCP and applicable domestic and international regulations. This may be a hospital, clinic, community health facility, private practice or health maintenance. A fully-fledged CRS in a clinical setting should have a CRS clinic with consultation rooms for the research participants, a triage, a treatment room for examination and other clinical operations units. Other CRS units include the CRS laboratory, approved by DCLOT to serve the network studies, the CRS clinical quality management (CQM) unit, the CRS regulatory team, and the CRS pharmacy. While a CRS pharmacy is part of a CRS, it should have an IMP repository, dispensing area, and study product or IMP preparation area operated by trained and registered professionals.

OHRP provides the federal wide assurance (FWA) to protect the rights, welfare, and well-being of human subjects in research. The FWA requires institutions to have written procedures for reporting to the IRB and U.S. federal agencies conducting or supporting the research.

FWA also requires institutions to support the IRB, rely on external IRBs if necessary, and renew the FWA.

To achieve these activities, the CRS are under direct oversight by the institutional review boards, regulatory ethical committees, plus other regulatory authorities (IRB/REG)-these review research protocols for the CRS and their data. National regulatory authorities and other in-country entities provide this oversight, including approval of clinical trials.

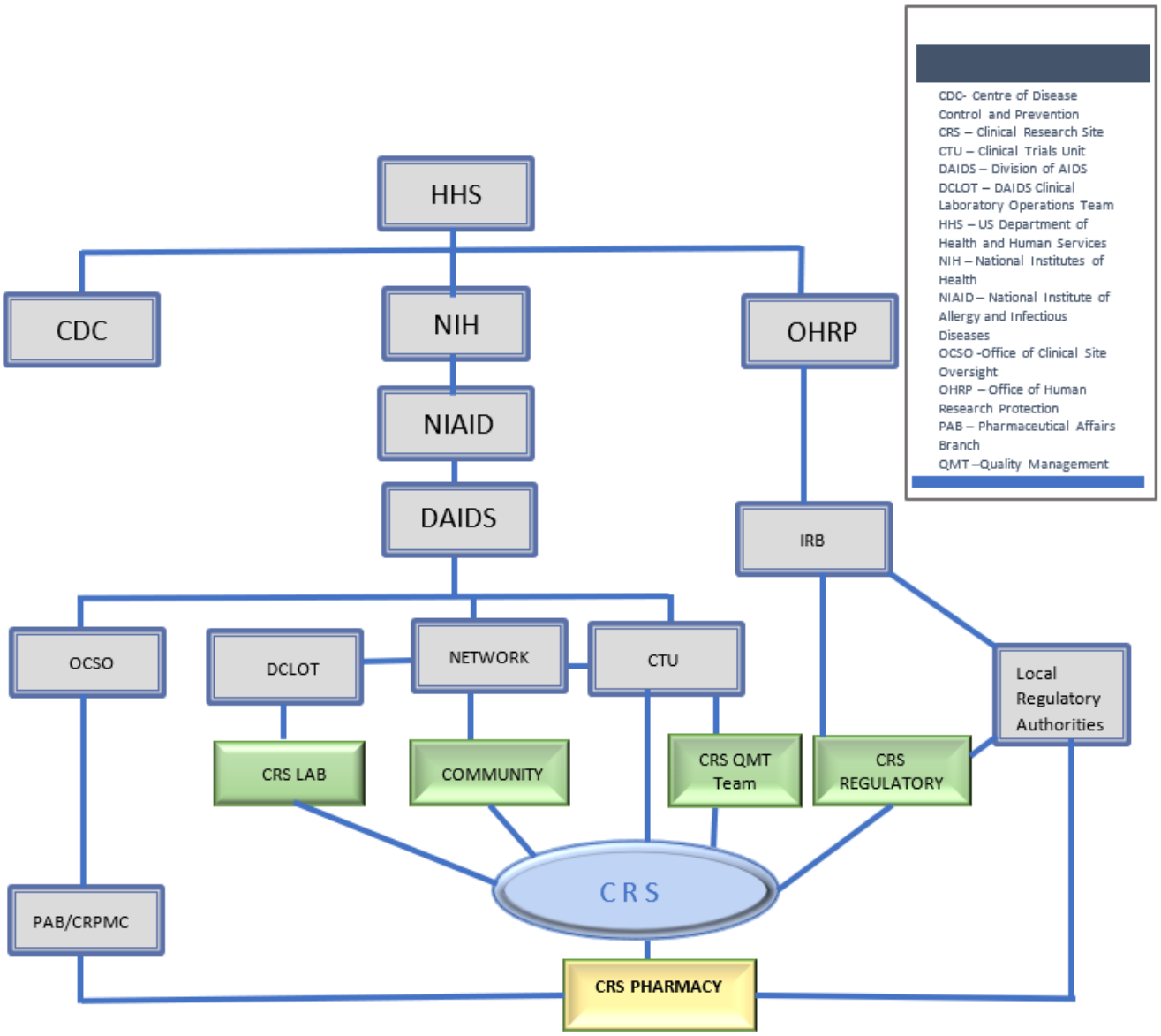

Figure 1: Interaction of the CRS with funding and administrative institutions.

LEGISLATIVE FRAMEWORK FOR COMMUNITY AND CRS PHARMACIES IN UGANDA

The national drug authority (NDA) licenses all medicine outlets in Uganda. NDA ensures that pharmacy operations are legitimate and that essential and cost-effective drugs are available to the entire population of Uganda.[8] Pharmacy operations must be suitable and secure, and an annual operation license from NDA is required.[18] CRS pharmacies apply for their operation licenses as retail or wholesale pharmacies, but there is no provision for them to submit their applications via the NDA management information system (NDAMIS). Pharmacists in CRS pharmacies receive additional training to achieve competence in supporting DAIDS-sponsored clinical trials. The PAB approves a CRS pharmacy's establishment and operations and, for smooth operations, assigns a pharmacist to work closely with the CRS pharmacists during the implementation of these studies. The CRS pharmacists must follow the recent DAIDS pharmacy guidelines, the laws and regulations of the US food and drug administration and national institute of health (NIH), the study protocol, the manual of operations, and the country-specific guidelines for their operation and guidance. They uphold ethical and

research principles for participant safety and well-being during the studies.

HOW CRS PHARMACIES DIFFER FROM COMMUNITY PHARMACIES

There are notable distinctions between community pharmacies and CRS pharmacies. These differences entail the type of population they cater to, the regulations they must comply with, the medical supplies they offer, the sponsors and support they receive, the personnel and their proficiency, and the management of these medical supplies (Table 1). Unlike community pharmacies, CRS pharmacies prioritise GCP and human subject protection (HSP) principles for participant safety and accurate data collection.[14,16,19] Community pharmacies strive to provide customers with the best possible care and service, offering advice and support when required to create a positive customer experience and build long-term trust and loyalty. Additionally, community and CRS pharmacies differ in how they interact with various agencies.

Entrance to a CRS pharmacy is restricted to study pharmacy staff to ensure privacy and confidentiality, especially in blinded clinical trials. They use biometric systems and CCTV cameras to buffer security. Conversely, in community pharmacies, customers may enter as they wish as long as the facility is open and operating.

Category CRS pharmacies/IND community pharmacies

Highlighting differences in target populations, regulations, drug supplies for the target populations, support, and sponsors, including the personnel working in these pharmacies. Regulators and practitioners in health settings and clinical research lack information about these differences.

Table 1: Comparison between CRS pharmacies and community pharmacies.

Population	Established for a CRS and serves research participants	Wholesale or retail pharmacies services for the community
Regulation	Regulated by both local, national (NDA) and external/international agencies	Regulated by local agencies: NDA
Medical supplies	IND or study products for the research participants	Registered and approved pharmaceutical products
Sponsors and support	NIH, pharmaceutical agencies	Privately owned, public or faith based-organizations
Personnel	Pharmacists or staff with a pharmacy background	Staff with a pharmacy or nursing background
Client-returns	Prior approval by sponsor or clinical research associate or DAIDS authorized witness	No prior approval is required.

ADDITIONAL REQUIREMENTS OF CRS PHARMACIES

Regulatory and sponsor requirements

NDA requires that research institutions seek NDA's approval before conducting clinical trials[20]. The research institution completes a clinical trial application form. When completing this application, the site pharmacist provides vital information and guidance to the institution's regulatory unit. Details about the requirements can be found on the NDA website. The NDA issues a clinical trial certificate (CTC) to the site as approval for the application. The CTC is valid for one year and should be renewed periodically based on the duration of the study. The site principal investigator (PI) must provide NDA with updates on the progress of the study, IMP-related issues, and any changes to the study's conduct. The site pharmacists support the site PI and provide any updates related to the study product management to the site PI. NDA inspects the facility annually to ensure the trials align with GCP and HSP. It's the responsibility of the site pharmacists to ensure that the CRS pharmacy meets the requirements of the National Regulatory Authority in as much as the site PI holds the ultimate responsibility of the clinical trial under inspection.

The world health organization (WHO) and the international pharmaceutical federation (FIP) have published Joint guidelines to ensure and improve quality pharmacy practices, considering the benefactors of these services.[4] The guidelines provide the competencies of the pharmacists, appropriate storage of medicines and information to the patients and monitoring and evaluation of the established systems of good pharmacy practices.[13,19] While these guidelines benefit pharmacy practices in various ways, regulatory oversight for monitoring and evaluating their impact is still challenging, especially in community pharmacies. Often, regulatory authorities lack sufficient resources to monitor the implementation of these practices in community pharmacies. In contrast, sponsors for the clinical trials contract teams to monitor the conduct of their studies at the sites at least annually or quarterly, including the CRS pharmacies. Institutional review committees are also mandated to conduct site inspections where the clinical trials are conducted.

The setup of a CRS pharmacy should enhance a unidirectional flow from the IMP storage to the preparation, dispensing, and administration of the pharmacist-prepared participant-specific study product. This limits traffic but also efficiently uses the available space. The site pharmacist should maintain the patients' or participants' privacy and confidentiality.

From IMP shipments to the study participants

Many institutions have learned during the COVID-19 pandemic that digitalising systems are efficient and effective.[21,22] In Uganda, the NDA established an online NDA Management Information System (NDAMIS) for renewing licenses, generating invoices, applying for permits, and verifying certificates for incoming study shipments. The site pharmacist uses this platform to send shipping documents with relevant information to the NDA, the regulatory authority. Importing entities need two crucial documents from the NDA: the annual import permit and the verification certificate. Among community pharmacies, wholesale pharmacies are usually involved in importing medicines. Retail pharmacies rarely do so. However, CRS pharmacies are actively importing IMP and, therefore, need approval from the regulators to bring in supplies. As such, CRS pharmacies need annual import permits and verification certificates for these shipments.

The annual import license permits the site to import IMP and other supplies but is not specific to a shipment. The verification certificate authorises the shipper to airlift a consignment from the shipper’s destination to the importer’s destination country. Both documents are required to import IMP and other study-related supplies. The site pharmacist is responsible for processing and securing these documents for the shipper via the NDAmis platform. To process a verification certificate, the site pharmacist needs shipping documents, such as a donation letter from the study's sponsor, manufacturer's details of the items in the shipment, invoice, packing list, certificate of analysis, and NDA clinical trials approval or certificate.

CRPMC is the custodian of the shipping documents, and they email them to the sites when all contractual obligations between the manufacturer and the study sponsor have been met. CRPMC receives a notification when a site is fully registered for a protocol. At this point, CRPMC sends the shipping documents to the site pharmacist, who uses them to obtain a verification certificate from the regulator for the shipper. The guidelines require that the site pharmacist conduct stock-level reviews during routine physical counts. This way, the site pharmacist can establish the prevailing gap in stock levels and prevent IMP stockouts by using lead time and submitting timely orders. IMP stockouts can affect the continuity of the study. Site pharmacists are responsible for establishing demand, forecasting IMP, submitting IMP orders to the CRPMC via the CRPMC online site management and ordering system (COSMOS), and ensuring sufficient study supplies at the site. Site pharmacists work with the sponsor and shipping agents to seek regulatory approval for the shipments. Additionally, the site pharmacist works with the clearing agent to secure release for the consignment.

Ideally, the consignment is packaged with data loggers to keep track of the temperature conditions during transit. Upon receipt of IMP at the CRS, the site pharmacist must download and upload the temperature monitoring device's temperature reports and notify the shipper. IMP should be stored according to the manufacturer's recommendations. IMP should be entered on the study product accountability forms upon receipt. Dispensing of IMP requires a prescription from an authorised prescriber. All source documentation and completion of the CRS Pharmacy tools for IMP accountability and dispensing should follow the principles of ALCOA+C (Attributable, legible, contemporaneous, accurate, and complete). During dispensing of IMP, the site pharmacist updates the CRS pharmacy tools (study product accountability log, participant worksheet if required, the chain of custody form for participants in a blinded study or instances where IMP is not dispensed directly to participants in the CRS pharmacy), IMP adherence assessment form, and the dispensing review form. The participant's original prescription, worksheet, and other pharmacy-related source forms are retained in the participant's pharmacy binder, while copies are filed in the study participant's clinic file.

Quality assurance and quality control

In DAIDS-sponsored clinical trials, the PoR establishes a pharmacy quality management plan (PQMP) as part of good pharmacy practice. The PQMP includes a quality control and quality assurance (QC/QA) system, ensuring consistency in compliance with the protocol, study-related documents and standard operating procedures. It outlines the personnel and their responsibilities, the QC/QA activities, corrective and preventive actions resulting from non-conformances and protocol deviations, required training, and evaluation of PQMP performance. The CRS leader or designee should approve the PQMP, which should be updated as needed.

All CRS pharmacies must have a PQMP, and DAIDS requires that staff receive mandatory training related to protocol implementation, as listed in Table 2.[15] These training pieces include GCPs, HSP, CQM plan, corrective action protective action (CAPA) for pharmacy staff, essential documents, source documentation, DAIDS clinical trials networks pharmacy guidelines training, monitoring 101, clinical site monitoring system, and inspection awareness and preparedness. They are part of the quality control and quality assurance system. These include the professional bodies and local regulatory training requirements.

Table 2: Pieces of required training for community and CRS pharmacists.

Pieces of training	Community pharmacists	CRS pharmacists
List of required trainings	Professional courses, Industrial training, internships and 40 structured continuous professional development hours per year	GCP, HSP, CQMP, CAPA for pharmacy staff, essential documents, source documentation, DAIDS clinical trials networks pharmacy guidelines*
Facilitating bodies/ institutions	Professional bodies and national regulatory authority	DAIDS and pharmaceutical sponsors

*****In addition to the training required by community pharmacists, CRS pharmacists must also complete additional training.

Training documentation for CRS pharmacy staff is kept in the pharmacy regulatory binder and must be available to monitors and inspectors when requested. The PoR is responsible for oversight and ensuring all pharmacy staff receive this training. Pharmacy staff must be qualified by pharmacy education, training and experience to perform their respective tasks. The PoR must ensure that all pharmacy staff are trained in all protocol-related and standard operating procedures training. In CRS pharmacies dispensing injectable study products, the PoR must organise annual refresher training in sterile drug preparation and hazardous drug management training for all pharmacy staff at least once a year, as per PAB. All training is documented, signed, dated and filed with the regulatory binder for inspection by monitors or inspectors.

CRS pharmacy monitoring and inspection

Monitoring is a process of ensuring that established procedures for a clinical trial are being followed, while inspection is an official review of documents, records, or facilities by regulatory bodies to assess the quality of data generated from clinical trials or ensure the safety and well-being of participants.

In DAIDS-sponsored clinical trials, monitoring is conducted by the OCSO, responsible for maintaining clinical research standards and ensuring adherence to policies and procedures.[10] The OCSO conducts network activities, including site establishment, periodic or closure visits, and site performance and administration issues. CRS Pharmacies supporting DAIDS-sponsored clinical trials undergo several sponsor-initiated monitoring visits, including protocol-specific investigational drug audits (PSIDA), investigational pharmacy inventory and storage assessments (IPISA), and annual pharmacy operations visits.

The PSIDA assesses pharmacy personnel, protocol records and documents, dispensing or preparing IMP, authorised prescribers, and any follow-up issues from previous visits. While as, the IPISA assesses investigational pharmacy personnel, accountability of the IMP, and any follow-up issues from earlier visits. To prevent unblinding study staff, the IPISA reports are shared with only DAIDS PAB and the PoR during a debrief session, while the monitor may share feedback from the PSIDA report with the rest of the CRS staff.

In contrast, inspection audits are less frequent but more thorough and are conducted by regulatory bodies such as the FDA, EMA, or drug regulatory authorities.[23,24] Inspectors are not required to provide debriefing sessions to study staff. During monitoring visits, the monitor calls for a debriefing meeting with the rest of the study staff and shares any findings from the visit.

Since the COVID-19 pandemic, remote source review (RSR) has become more prevalent and necessary for regulatory assessments. RSR allows more efficient and flexible monitoring and reduces sponsors' travel costs. DAIDS has provided compliant RSR platforms to all DAIDS-supported sites, including the medidata RSR platform, which is available at no additional cost and provides staff with the same login as medidata rave EDC, study-specific visit folders and preconfigured pharmacy folders with specific study requirements to prevent unblinding.[25]

CRS pharmacy power supply, equipment and maintenance

It is essential to emphasise the storage of IMP at the recommended temperatures in the operation of a CRS pharmacy. This is essential for avoiding study product deterioration, which has the potential to impact study product efficacy and safety.[26] A CRS pharmacy cannot rely solely on the national power grid. In LMIC, which is faced with power surges, this challenge can be addressed using multiple power sources.[27] In addition to the national grid, the CRS should have a standby generator and a backup to the standby generator to complement the power supply. The power sources should be arranged in parallel to support each other. This could be achieved using automatic transfer switches (ATS) and an electricity distribution board (DB), as illustrated in Figures 2 A and 2 B. The distribution board isolates the connections to each piece of equipment in the CRS pharmacy. By having multiple power sources arranged in parallel, the possibility of power outages can be minimised to zero, creating a reliable power supply for 360 days a year, a desired condition for IMP storage in a clinical trial.

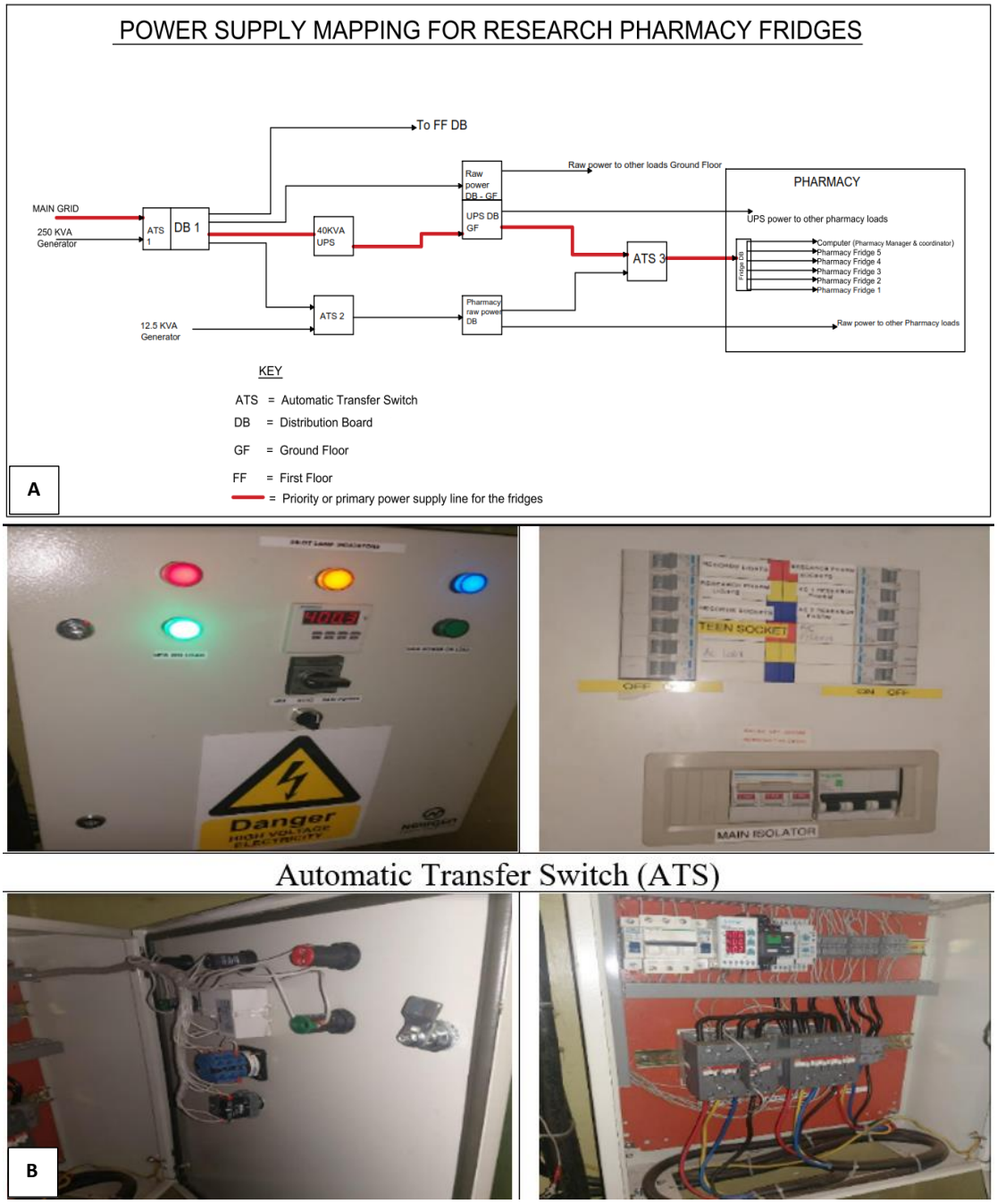

Figure 2 (A and B): Power distribution to equipment in the CRS pharmacy and components of the ATS.

A: The power sources for the CRS pharmacy equipment include the national grid, standby generator, and backup to the standby generator. B: The ATS is part of the power supply map in Figure 2 A. It facilitates the transfer of power sources, such as from the primary national grid to the standby generators (ATS1, 250 KVA generator) when there is a blackout from the national grid or the standby generator to the backup of the standby generator (ATS2, 12.5 KVA generators). ATS3 facilitates the power supply transfer from the 40 KVA UPS to the 12.5 KVA generator.

The equipment in a CRS pharmacy can range from refrigerators and freezers to biosafety cabinets or isolators, depending on the capacity and clinical trials conducted at the site. It is preferred for a CRS pharmacy to have primary and secondary equipment during the conduct of cutting-edge clinical trials. The secondary or backup is part of a contingency plan, providing continuity in case of a breakdown and support if the primary equipment is under routine service maintenance, and vice versa.

In clinical research, pharmaceutical refrigerators and laboratory freezers are preferred over domestic brands. Storage of investigational products within the manufacturer's recommended temperature ranges is critical for their efficacy. Therefore, pharmaceutical-grade freezers and refrigerators are equipped with

microprocessor-based temperature control, digital temperature sensors and powerful fans that promote uniform distribution and fast temperature recovery to maintain the investigational products with the manufacturer's recommended storage temperature. Each IMP storage equipment, freezer, and refrigerator should be monitored with a primary and secondary temperature monitoring device.

Pharmaceutical-grade refrigerators and freezers without an alarm notification system may still compromise standards, especially in settings with unstable power supply. Several alarm notification systems have been suggested, including visual, audible, SMS messages/ emails, and telephone alert calls or alarms (Table 3). Telephone alert calls are preferred to other notification systems for on-site and off-site temperature monitoring. DAIDS PAB requires that CRS pharmacies monitor and report for temperature excursions.

Table 3: Alert notification systems.

Notification alerts	Signals to environmental changes
Visual alarms	The presence of lights is an alert. It may require periodic checks by staff and may result in delays.
Audible	It is linked to the temperature monitoring system, which alerts staff about on-site excursions. The alarm should be audible so that staff can receive the alert and respond to the excursion.
SMS message/ email	Linked to a local server or network and send automated alerts to staff in the event of an excursion
Voice phone calls	It is also linked to the network but provides precise real-time status about temperature changes, power failures, and equipment status by directly calling staff on and off-site. The messages are customised to identify the affected destinations or zones.

There is a gradual shift from oral to injectable products in HIV/AIDS treatment and prevention in the clinical research arena.[28] Research pharmacists at the CRS use a septic technique or vial adapters to prepare these products.[29] However, these skill sets are neither taught in pharmacy training nor enforced by the regulatory authorities. As such, these are novel skills to the pharmacy profession yet are becoming relevant to practice. This kind of equipment undoubtedly has an enormous financial investment, from its acquisition, equipment qualification, validation, certification, and supplies, which may vary depending on the type and manufacturer's recommendations.

Routine service maintenance and quality of health services go hand in hand, so validation and calibration of this equipment must be routinely conducted.[30] The pharmacy team must develop a service tracker for routine service and maintenance. The site pharmacists are responsible for monitoring the availability, stock levels, and potential sources of the physical protective gear (PPE) for the continuity of the study's implementation. Community pharmacies and other settings where the products are administered may find it challenging to implement since most of them are profit-oriented. In clinical research, CRS managed to subside the high maintenance costs by synchronising activities and cost-sharing.[31]

DISCUSSION

CRS pharmacies differ broadly from community pharmacies in their target population, operation, and setup. These differences are unnoticed by regulators because CRS pharmacies are still few, and none are keenly interested. As such, the local regulators are bound to enact guidelines that do not fully align with their operations and practice. Secondly, the CRS pharmacy field is still growing compared to other pharmacy areas of operation, like community pharmacy practice. Training institutions are also an excellent place to foster these skill sets for practitioners.

CRS pharmacists are responsible for ensuring that participants on various protocols receive the right IMP in the correct dose at the right time with the appropriate instructions. In some situations, the drive for using computerised provider order entry (CPOE) and clinical decision support systems (CDS) is to minimise the chances of medication errors, especially in these populations.[32,33] However, these systems are not yet feasible and sustainable in resource-limited settings. As an alternative, CRS pharmacists adopt cost-effective tools for inventory management, prescribing, dispensing and administering study products to minimise the chances of medication errors and meet age, population and study-specific demands. These approaches are affordable and more sustainable in resource-limited settings than CPOE and CDS since they do not require huge investments.

This review is limited due to the lack of information about CRS pharmacies. Nonetheless, the article highlights compelling differences for the policy makers and regulators. We did not explore some areas of practice involving participants' opinions and tracking their process during the study compared to clients who access services in community practice. Other than the traditional dispensing and client counselling services provided by community pharmacists, this review did not explore other specialized services such as the transition of care, managing chronic medication, their role in community interventions, screening public health conditions and other health-related activities.

CRS pharmacists should be highly organized and agile because they deal with several stakeholders and varying

demands during clinical trials. Secondly, CRS pharmacists should be receptive to gaining new knowledge and skills, as various protocols have different requirements. Some of the practices in CRS pharmacies could benefit community pharmacies. These could be achieved through training and amendments to the policy and guidelines. If this is desired, pharmacists in community practices would also take up additional roles. Several authors have cited the need for training in community pharmacies.[34,35] This could improve the quality of health service delivery to the community.

It is crucial to recognize the benefits of incentivizing and supporting implementation in community pharmacies of routine practices in CRS pharmacies, such as a 24-hour electricity supply through back-ups and strict temperature monitoring. These practices ensure the quality and safety of medications and contribute to the community's overall health and well-being. These facilities store and distribute public health commodities such as vaccines, the efficacy of which has significant public health implications. Other practices like proper record keeping can prove to be vital along all levels of the supply chain in the events of counterfeits or drug recalls, underscoring the necessity of these actions.

Regulators should not treat community pharmacies and CRS pharmacies in the same way. Community pharmacies serve the public by providing medication and health advice, while CRS pharmacies are involved in developing new drugs and medical treatments. Recognizing these differences would lead to better regulation and licensing practices, ultimately improving the quality of health services provided to the community and working with the existing CRS to sharpen the guidelines and policy, use of the CRS pharmacies as model centres or placement for the trainees and provision of targeted CPD programs to improve competencies through knowledge sharing. As part of their crucial mandate, pharmacy councils, regulators and training institutions in LMICs should take the lead in this role to improve the most underserved areas of pharmacy practice.

CONCLUSION

In summary, CRS pharmacies in LMIC are unique in their requirements, operation, service, and setup compared to community pharmacies. Regulatory authorities should formulate policies and guidelines that align with the operations of CRS pharmacies. They should also adopt good practices and utilize the existing CRS pharmacies to impart skills and knowledge to trainees and community pharmacies. This will promote the delivery of quality health services to the community.

ACKNOWLEDGEMENTS

Authors would like to thank to CTU consultant, Vivian Rexroad, and the CTU coordinator, Mahnaz Motevalli, for their support in setting up the Baylor Uganda CRS pharmacy. Also, to engineers Isaac E. Luke Enyenu and Harun Mugabe for their technical assistance, Rachel Kikabi Namuddu, Susan Tukamuhebwa, and Henry Balwa for their general support, and the PAB protocol pharmacists, Lynette Purdue, and Katherine Shin, for their unwavering efforts in assisting the site pharmacists in conducting DAIDS clinical trials.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Bickel RJ, Curtis DC, Richard LL, James GS, Kathleen P, Terry JB, et al. Moving the pharmacy practice model initiative forward within a state affiliate. Am J Health-System Pharmacy. 2014;71(19):1679-85.
2. Toklu HZ, Hussain A. The changing face of pharmacy practice and the need for a new model of pharmacy education. J Young Pharmacists. 2013;5(2):38-40.
3. Atkinson J. Advances in Pharmacy Practice: A Look towards the Future. Pharmacy. 2022;10(5):125.
4. Unhurian L, Bielyaieva O, Vyshnytska I, Suschuk N, Petkova I. Implementation of standards of good pharmacy practice in the world: A review. Asian J Pharmaceutics. 2018;12(1):S42.
5. Babar ZUD. Ten recommendations to improve pharmacy practice in low and middle-income countries (LMICs). J Pharmaceut Policy Practice. 2021;14(1):6.
6. Ambler S, Sheldrake L. Pharmacy practice research: challenges and opportunities. Prim Health Care Res Dev. 2009;10(1):4-6.
7. Garcia-Cardenas V, Charlotte VR, Fernando FL, Martin S, Ross T, Olivier B, et al. Pharmacy practice research-A call to action. Res Social Adm Pharm. 2020;16(11):1602-8.
8. The national drug policy and authority act. The Law Reform Commission of Uganda. Uganda National Drug Policy and Authority Act. 2016;8:2-46.
9. National Drug Authority. Licensed Outlets Statistics. 2024. Available at: https://www.nda.or.ug/licensed-outlets-statistics/. Accessed on 10 June 2024.
10. NIH, National Institute of Allergy and Infectious Diseases and DAIDS. HIV/AIDS Clinical Trials Networks. Available at: https://www.niaid.nih.gov/research/hivaids-clinical-trials-networks. Accessed on 10 June 2024.
11. The Republic of Uganda. The Uganda Gazette. 2019. Available at: https://gazettes.africa/akn/ug/officialGazette/government-gazette/2019-11-08/57/eng@2019-11-08p2284-2289. Accessed on 10 June, 2024.
12. Danielson J, Kathleen HB, Cheryl C, Deb C, Denise MK, Lena M, Kate N, et al. Essential elements for core required advanced pharmacy practice

experiences. Am J Pharmaceutical Educ. 2019;83(4):6865.
13. Federation International Pharmaceutical. Good Pharmacy Practice (GPP) in developing countries. Recommendations for stepwise implementation. 1997. Available at: https://www.fip.org/files/fip/Statements/GPPrecommendations.pdf. Accessed on 10 June 2024.
14. Division of AIDS Pharmaceutical Affairs Branch. Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks. 2023. Available at: https://www.niaid.nih.gov/sites/default/files/wa09_pharmacy_guidelines_02aug2023_final.pdf. Accessed on 10 June 2024.
15. National Institute of Allergy and Infectious Disease (NIAID). Division of AIDS (DAIDS) Site Clinical Operations and Research Essentials (SCORE) Manual: Pharmacy Requirements. Available at: https://www.niaid.nih.gov/sites/default/files/score-pharmacy-requirements.pdf#:~:text. Accessed on 10 June, 2024.
16. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). Integrated addendum to ICH E6(R1): guideline for good clinical practice E6(R2). International Council for Harmonization. 2016. Available at: https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf. Accessed on 10 June 2024.
17. Vijayananthan A, Nawawi O. The importance of Good Clinical Practice guidelines and its role in clinical trials. Biomed Imaging Interv J. 2008;4(1):e5.
18. The Pharmaceutical society of Uganda. Standard of Pharmacy Practice for retails Pharmacies in Uganda, Edition 2014. Available at: http://psu.or.ug/wp-content/uploads/2022/10/Standards-of-Pharmacy-Practice-Retail.pdf. Accessed on 10 June, 2024.
19. Shrestha R, Ghale A. Study of good pharmacy practice in community pharmacy of three districts of Kathmandu valley, Nepal. Int J Scientific Rep. 2018;4(10):240-5.
20. The National Drug Authority. Guidelines on Good Clinical Practice in the conduct of clinical trials involving Human Participants. Doc no. DPS/GDL/025. 2019. Available at: https://www.nda.or.ug/wp-content/uploads/2022/02/Good-Clinical-Practice.pdf. Accessed on 10 June 2024.
21. Fu Z, Liu X, Zhao S, Yuan Y, Jiang M. Reducing Clinical Trial Monitoring Resources and Costs with Remote Monitoring: Retrospective Study Comparing On-Site Versus Hybrid Monitoring. J Med Internet Res. 2023;25:e42175.
22. Abidi N, Sakha S, El Herradi M. Digitalization and Resilience: Firm-level Evidence During the COVID-19 Pandemic. Telecomm Policy. 2022;47(4):102522.
23. Lawrence CS. FDA Inspection of Clinical Research Sponsors and Investigators: Avoiding the Pitfalls. Ther Innov Regul Sci. 1988;22:753-64.
24. Sellers JW. Descriptive Analysis of Good Clinical Practice Inspection Findings from U.S. Food and Drug Administration and European Medicines Agency. Ther Innov Regul Sci. 2022;56:753-64.
25. Office of Clinical Site Oversight. Monitoring Operations Branch newsletter. Available at: https://www.hanc.info/content/dam/hanc/documents/daids/mob-newsletters/MOBReport17thEdition_Dec2021.pdf. Accessed on 10 June 2024.
26. Yu YB, Briggs KT, Taraban MB, Brinson RG, Marino JP. Grand Challenges in Pharmaceutical Research Series: Ridding the Cold Chain for Biologics. Pharm Res. 2021;38(1):3-7.
27. Muliyati D, Bakri F, Umami I, Sumardani D, Ambarwulan D. The generator operating system automatically uses a motorized change over switch devices. J Physics: Conference Series. 2019;1402(4):044010.
28. Kim YS. Long-Acting Injectable Antiretroviral Agents for HIV Treatment and Prevention. Infect Chemotherapy. 2021;53(4):686-95.
29. European Medicines Agency. European Medicines Agency. Annex 1: Summary of product characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/vocabria-epar-product-information_en.pdf. Accessed on 10 June 2024.
30. Zamzam AH, Ahmad KAW, Muhammad MA, Suresh CS, Khin WL, Khairunnisa H. A Systematic Review of Medical Equipment Reliability Assessment in Improving the Quality of Healthcare Services. Front Public Health. 2021;9:753951.
31. Whistler T, Kaewpan A, Blacksell SD. A biological safety cabinet certification program: Experiences in southeast Asia. Applied Biosafety. 2016;21(3):121-7.
32. Ruutiainen H, Kunnola E, Holmström A, Kuitunen S. 5PSQ-108 Computerised physician order entry with clinical decision support in preventing wrong dose errors in paediatric medication orders: a systematic review. Paediatr Drugs. 2023;26(2):127-43.
33. Mogharbel A, Dowding D, Ainsworth J. Physicians' use of the computerized physician order entry system for medication prescribing: systematic review. JMIR Med Info. 2021;9(3):e22923.
34. Asmelashe Gelayee D, Binega Mekonnen G, Asrade AS. Practice and Barriers towards Provision of Health Promotion Services among Community Pharmacists in Gondar, Northwest Ethiopia. Biomed Res Int. 2017;2017:7873951.
35. Bou-Saba AW, Kassak KM, Salameh PR. The current trends and challenges towards good community pharmacy practice and the way forward. Explor Res Clin Soc Pharm. 2022;6;100152.

Cite this article as: Sekabira R, Murungi G, Kinyera NO, Kisekka MN, Korutaro V, Nahirya PN, et al. A clinical research site pharmacy for the division of AIDS sponsored clinical trials in a low-middle-income country. Int J Sci Rep 2024;10(8):286-95.